

## **REMARKS**

This amendment is responsive to the Office Action mailed October 28, 2008. Claims 1-52 are pending of which claims 5-10 and 22-49 are withdrawn. In the present paper, claims 2-3, 5-10 and 22-49 are canceled without prejudice as explained below. Claims 1, 4, 11-21, and 50-52 are amended. New claim 53 has been added. Thus, following entry of the present amendment, claims 1, 4, 11-21, and 50-53 will be pending and under consideration.

### **I. AMENDMENTS TO THE SPECIFICATION**

The paragraphs beginning on page 3, line 4; page 25, line 9; and page 25, line 15 are amended to provide the correct figure number that corresponds with the description. Support for the amendments may be found, for example, in the specification at page 3, lines 1-3, and Figure 1C, as originally filed.

The amendments to the specification are fully supported by the specification and figures as originally filed, and thus, these amendments present no new matter. Applicants respectfully request entry of the amendment to the specification.

### **II. AMENDMENTS TO THE CLAIMS**

Claims 5-10 and 22-49 directed to non-elected subject matter and claims 2-3 have been canceled without prejudice to Applicants' rights to pursue the canceled subject matter in one or more continuation or divisional applications.

Claims 1, 4, 11-21, and 50-52 have been amended. Support for the amendments to claims 1, 4, and 11-14 may be found, for example, in the specification at page 2, lines 10-12, and page 18, lines 1-7, as originally filed. Support for the amendments to claim 15 may be found, for example, in the specification at page 2, lines 10-12, and page 14, lines 3-5, as originally filed. Support for the amendments to claims 16 and 17 may be found, for example, in the specification at page 2, lines 10-12, page 3, lines 1-3, page 6, lines 16-19, page 7, lines 17-19, page 16, lines 1-9, page 18, lines 1-7, and page 21, lines 12-13, as originally filed. Support for the amendments to claim 18 may be found, for example, in the specification at page 2, lines 10-12, and page 14, lines 12-14, as originally filed. Support for the amendments to claims 19-21 may be found, for example, in the specification at page 13, lines 18-28, as

originally filed. Support for the amendments to claims 50-52 may be found, for example, in the specification at page 2, lines 10-12, page 19, lines 23-32, as originally filed.

New claim 53 is supported, for example, by the specification at page 14, lines 3-5, as originally filed.

As the amendments to the claims are fully supported by the application as filed, they present no new matter. Accordingly, entry of the present amendments to the claims is hereby respectfully requested under 37 C.F.R. § 1.111.

No claim amendment fee is believed to be due with these amendments.

### **III. REPLACEMENT DRAWINGS**

Attached in Appendix A are seven replacement sheets of drawings comprising Figures 1-3 to be substituted for the original three sheets of informal drawings presently on file for the above-identified application. Figures 1-3 have each been redrawn on multiple sheets (Figure 1A, Figure 1B, etc.) in order to enlarge portions of the drawings and to make them legible. Shading is removed from Figures 1B, 2A, and 3B. Boxes encompassing Figures 3A and 3C are removed. Each sheet of drawings is labeled "REPLACEMENT SHEET".

Italian words appearing on Figures 1B, 2A, 3B, and 3C have been amended to the corresponding English words according to the English translation of Italian Application No. MI2003A001156, to which the instant application claims priority. Specifically, in Figures 1B, 2A, and 3B, the Italian word "Controllo" has been amended to the English word "Control", and the Italian word "Malato" has been amended to the English phrase "Affected subject". In Figure 3C, the Italian word "esone" has been amended to the English word "exon", the Italian word "Cambio" has been amended to the English word "Substitution", the Italian word "Asparagina" has been amended to the English word "Asparagine", the Italian word "Isoleucina" has been amended to the English word "Isoleucine", the Italian word "Idrofilico" has been amended to the English word "Hydrophilic", the Italian word "Idrofobico" has been amended to the English word "Hydrophobic", and the Italian phrase "Non carico" has been amended to the English word "uncharged". Support for the amendments may be found, for example, in Figures 1B, 2A, 3B, and 3C of the English translation of Italian Application No. MI2003A001156, which is submitted herewith.

Applicants respectfully submit that the amendments to the drawings are in compliance with 37 C.F.R. §§ 1.84 and 1.121(d).

The amendments to the drawings are fully supported by the application and drawings as originally filed and thus present no new matter. Applicants respectfully request entry of the replacement drawings.

#### **IV. PRIORITY**

The instant application claims priority to Italian Application No. MI2003A001156, which was filed on June 9, 2003. Attached hereto in Appendix B are an English translation of Italian Application No. MI2003A001156 and a statement by the translator that the English translation of Italian Application No. MI2003A001156 is accurate. Entry of these documents to the record is respectfully requested. Applicants respectfully submit that these submissions are in accordance with 37 C.F.R. § 1.55 and accordingly, the instant application is entitled to a priority date of June 9, 2003.

#### **V. OBJECTION TO THE DRAWINGS**

The Patent Office objects to the drawings allegedly because the drawings are not legible. Attached in Appendix A are seven (7) replacement sheets of drawings for Figures 1-3 to be substituted for the three (3) sheets of drawings presently on file for the above-identified application. Applicants respectfully submit that the objection to the drawings is overcome with the replacement drawings.

Applicants respectfully request withdrawal of this objection to the drawings.

#### **VI. OBJECTION TO THE CLAIMS**

The Patent Office objects to claim 16 under 37 C.F.R. § 1.75(c) as allegedly being of improper dependent form. The Patent Office alleges that certain SEQ ID NOs recited in claim 16 do not correspond to a portion of SEQ ID NO:3, which is recited in claim 15 to which claim 16 depends. Office Action, pages 3-4.

Without acquiescing to the propriety of the rejection, and solely to expedite prosecution of the claims, Applicants have amended claim 16 to recite the isolated polynucleotide according to claim 15 further comprising at least one of the oligonucleotide sequences of SEQ ID NO: 13 or 14. For instance, as supported by page 18, lines 2-7 of the specification as originally filed, the 421 bp amplification product comprises nucleotide position 238 of SEQ ID NO:3 and sequences of SEQ ID NO:13 or 14. As such, Applicants respectfully submit that this objection is obviated in view of the amendments to claim 16.

Applicants respectfully request withdrawal of the objection to claim 16.

**VII. CLAIM REJECTION UNDER 35 U.S.C. § 101 AS DIRECTED TO  
NON-STATUTORY SUBJECT MATTER**

---

Claims 15-17 stand rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. The Patent Office alleges that the claims do not recite an isolated polynucleotide molecule such that the claims would be directed to statutory subject matter. Office Action, page 4.

Without acquiescing to the propriety of the rejection, and solely to expedite prosecution of the claims, Applicants have amended claims 15-17 to recite “isolated polynucleotide”, as suggested by the Patent Office. As such, Applicants respectfully submit that this objection is obviated in view of the amendments to claims 15-17.

Thus, Applicants respectfully submit that the presently pending claims are directed to statutory subject matter. Accordingly, Applicants respectfully request that the rejection of claims 15-17 under 35 U.S.C § 101 be withdrawn.

**VIII. CLAIM REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR  
FAILING TO COMPLY WITH THE WRITTEN DESCRIPTION**

---

Claims 1-4, 11-14, 18-21, and 50-51 stand rejected under 35 U.S.C § 112, first paragraph as allegedly failing to comply with the written description requirement. The Patent Office alleges that Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species with the claimed genus. Office Action, pages 5-7. The rejection of claims 2-3 is moot in view of the cancellation of the claims.

Without acquiescing to the propriety of the rejection, and solely to expedite prosecution of the claims, Applicants have amended claim 1 to recite an isolated polynucleotide coding for a ferroportin 1 polypeptide comprising SEQ ID NO:2, wherein the glycine at position 80 of SEQ ID NO:2 is substituted with a serine. As such, Applicants respectfully submit that this rejection is obviated in view of the amendments to claim 1. Applicants respectfully submit that the written description requirement is met with respect to claims 1, 4, 11-14, 18-21, and 50-51.

Accordingly, Applicants respectfully request withdrawal of the rejection to claims 1-4, 11-14, 18-21, and 50-51 under 35 U.S.C § 112, first paragraph.

**IX. CLAIM REJECTION UNDER 35 U.S.C § 112, FIRST PARAGRAPH, FOR LACK OF ENABLEMENT**

---

Claims 1-4, 11-21, and 50-52 stand rejected under 35 U.S.C § 112, first paragraph, as failing to comply with the enablement requirement. The rejection of claims 2-3 is moot in view of the cancellation of the claims. Applicants respectfully traverse the rejection of claims 1, 4, 11-21, and 50-52.

At the outset, Applicants note that in this rejection the Patent Office specifically addresses the “how to use” aspect of enablement, or in other words, the rejection is one under 35 U.S.C § 101 for lack of utility since, for instance, the Patent Office alleges that “[t]he specification provides no evidence that the G80S mutation in the ferroportin 1 gene is associated with impaired [iron] homeostasis or hereditary hemochromatosis” (page 9); and that a “polynucleotide to the mutant allele does not appear to have any use unless the skilled artisan could assess the disease state of an individual” (page 10). The Patent Office alleges “that it would require undue experimentation for one of skill in the art to *perform the method of the claim* as broadly written.” Office Action, page 11 (emphasis added). Applicants note that the claims are not directed to methods, but to polynucleotides as well as vectors and kits comprising the polynucleotides, for which the sequences are provided. With respect to *compositions*, evidence of any utility is sufficient since the claims do not recite any particular utility. *See Nelson v. Bowler*, 206 U.S.P.Q. 881, 883 (CCPA 1980). Indeed, in *Nelson v. Bowler*, tests evidencing pharmacological activity for certain compositions were found to manifest a practical utility even though they may not establish a specific therapeutic use. *See Nelson v. Bowler*, 206 U.S.P.Q. at 883 (stating that “[p]ractical utility” is a shorthand way of attributing “real-world” value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public.”). As explained below, Applicants respectfully submit that the specification provides evidence of a specific, credible, and substantial utility for the claimed subject matter such that one skilled in the art can use the subject matter in a manner which provides immediate benefit to the public.

The ferroportin 1 gene (also termed SLC40A1) has a known sequence. The instant application provides the first disclosure of a ferroportin 1 gene mutation leading to a glycine to serine substitution in the ferroportin protein sequence (the G80S mutation), which was found in a family of G80S carriers, a family also characterized as having a high incidence of non-HFE hemochromatosis. *See* Specification, page 2, lines 23-28; page 21, line 1, to

page 22, line 5; and Figure 1. G80S mutation is an autosomal dominant mutation, *i.e.*, an individual carrying G80S mutation on one allele is necessarily affected by hemochromatosis. *See* Mougiou *et al.*, 2008, *Blood Cells, Molecules, and Diseases* 14:138-39; Wallace and Subramaniam, 2007, *World J. Gastroenterol.* 13(35):4690-4698 (copies are provided with the Information Disclosure Statement submitted herewith). Clinical traits associated with the G80S mutation are that its carriers have ferritinemia with ferritin levels of 1000-2000 ng/ml in untreated males and 700 ng/ml in females including elderly females of post-menopause age. Specification, page 8, lines 18-25. As a reference, normal serum ferritin levels have been measured at 94 ng/ml in males and 34 ng/ml in females. Cook *et al.*, 1974, *Am. J. Clin. Nutr.* 27:681-687 (a copy is provided with the Information Disclosure Statement submitted herewith). The specification provides that hemoglobin and ferritinemia values are not by themselves sufficient to provide per se a diagnostic indication of non-HFE hemochromatosis because of factors such as age and time of diagnosis. Specification, page 9, lines 23-28. Hence, the claimed subject matter would be of immediate benefit to ascertain if those individuals with abnormal hemoglobin and ferritinemia values are carriers of the G80S mutation, and thus, at risk for non-HFE hemochromatosis similar to the family of G80S carriers. *See* Specification, page 9, lines 23-27.

More so, those skilled in the art acknowledge the G80S mutation as having a real-world value as evidenced, for example, by a reference to the G80S mutation as one of the reported autosomal dominant mutations associated with hemochromatosis. *See* Figure 4 of Wallace *et al.*, 2007, *World J. Gastroenterol.* 13(35):4690-4698 (a copy is provided with the Information Disclosure Statement submitted herewith). The authors state that “[m]utations in these genes [including the ferroportin gene] occur in populations world wide and account for the majority of HH cases not linked to HFE. The study of these disorders has led to a greater understanding of how the body regulates iron homeostasis.” *See* Wallace *et al.* at page 4695, col. 2, last paragraph. Thus, for at least the reasons provided above, the claimed subject matter meets the requirements of utility under 35 U.S.C § 101, as well as the enablement requirement under 35 U.S.C § 112, first paragraph.

Nonetheless, to remove any doubt that no undue experimentation is required to practice the presently pending claims, Applicants address each of the factors from *In re Wands* that, when taken together, supports a finding of no undue experimentation.

### **The Legal Standard**

“The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without ‘undue experimentation.’” *Amgen Inc. v. Hoechst Marion Roussel*, 65 U.S.P.Q.2d 1385, 1400 (Fed. Cir. 2003). Enablement is not precluded by the necessity for some experimentation; the key word is “undue,” not “experimentation.” *See In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Factors to be considered in determining if experimentation is undue include the so-called “Wands factors” that include: the quantity of experimentation necessary; the amount of direction or guidance presented; the presence or absence of working examples; the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; and the breadth of the claims. *In re Wands*, 8 U.S.P.Q. 2d 1400, 1404 (Fed. Cir. 1988). These factors are presented in the order following that in the Office Action.

**1. The Nature of the Invention and The Breadth of the Claims**

The rejected claims are drawn to polynucleotides and vectors, cells, and kits comprising the recited polynucleotides. Since, for example, the specification provides sequences of the polynucleotides, these two *Wands* factors, the nature of the invention and the breadth of the claims do not support a finding of undue enablement to make and use the claimed subject matter.

**2. The Unpredictability of the Art, The State of the Prior Art**

The Patent Office contends that the prior art teaches genetic variations and associations are often irreproducible and that the specification provides no evidence that the G80S mutation in the ferroportin 1 gene is associated with impaired iron homeostasis or hereditary hemochromatosis. Office Action, pages 8-9. Applicants respectfully disagree.

As discussed in detail above, the specification provides that the G80S mutation is carried in a particular family having a high incidence of non-HFE hemochromatosis, and that clinical traits associated with being a G80S carrier include higher than normal ferritinemia values. The clinical traits associated with the G80S mutation are partially similar to those described in Pietrangelo *et al.* (*New England Journal of Medicine*, 1999, 341(10):725-732), caused by the mutation of amino acid 77 in the ferroportin sequence (A77D mutation) described in WO 02/033119. *See* Specification, page 5, lines 2-6 (copies of each of the cited references are enclosed with the Information Disclosure Statement filed herewith). Hence,

the state of the art provides that ferroportin mutations may in fact contribute to non-HFE hemochromatosis. Applicants respectfully submit that those diagnosed with hemoglobin and ferritinemia values outside of the normal range would find the recited polynucleotides of immediate benefit to ascertain for the possibility of being a G80S carrier, and thus, possibly at risk for non-HFE hemochromatosis similar to the family of G80S carriers. *See* Specification, page 9, lines 23-27. For these reasons, at a minimum, it is respectfully submitted that the unpredictability of the art and the state of the prior art are favorable to a finding that no undue enablement is required to make and use the claimed polynucleotides and vectors, cells, and kits comprising these polynucleotides.

**3. The Amount of Direction or Guidance Presented**

The specification provides sufficient guidance that enables one of skill to make and use the claimed subject matter in its full scope in a routine manner. The specification provides a detailed protocol for synthesizing the isolated polynucleotides recited in amended claim 1. Specification, page 21, line 1 to page 22, line 13. In particular, the working example provided in Example 1 teaches amplifying and sequencing the presently claimed isolated polypeptide from genomic DNA obtained from the hemochromatosis affected subjects, who carry the recited polymorphism. *Id.* Further, Example 3 teaches using the isolated polynucleotides of Example 1 to diagnose the hemochromatosis affected subjects based on the presence of the polymorphism at nucleotide 238 of the ferroportin 1 gene, which is detected by digestion with TspR1 restriction enzyme. Specification, page 25, lines 1-17; Figure 1. Taken together with the description of the clinical traits associated with the G80S mutation in the ferroportin 1 gene, which as explained above, the guidance presented in the specification, in light of the knowledge in the art, indicates that no undue experimentation is necessary to make and use the claimed subject matter.

The Patent Office alleges that “[t]he specification does not teach how to use the C or T variant in the nucleic acid.” Office Action, page 9.

Without acquiescing to the propriety of the rejection, and solely to expedite prosecution, Applicants have canceled claim 2 and amended claim 4 to recite the isolated polynucleotide according to claim 1, wherein nucleotide 238 of SEQ ID NO:1 is A. As such, Applicants respectfully submit that the allegation is obviated in light of the amendments to the claims. Moreover, amended claim 1 recites an isolated polynucleotide coding for a ferroportin 1 polypeptide comprising SEQ ID NO:2, wherein the glycine at position 80 of



SEQ ID NO:2 is substituted with a serine. The specification provides guidance on amplifying and sequencing the presently claimed isolated polynucleotides from genomic DNA obtained from the hemochromatosis affected subjects and control subjects. *See, e.g.*, Specification, page 21, line 1 to page 22, line 13. In particular, exon 3 of the ferroportin 1 gene, which encompasses the nucleotide position 238 that encodes the G80S mutation can be amplified by PCR using the primer pair, SEQ ID NO: 13 and 14. *Id.*

Accordingly, considering the amount of direction or guidance presented, warrants a finding in favor that no undue experimentation is required to make and use the recited polynucleotides and vectors, cells, and kits comprising the recited polynucleotides.

**3. The Relative Skill of Those in the Art and The Quantity of Experimentation Necessary**

---

With regard to the relative skill of those in the art, the Patent Office acknowledges that level of skill is high. Office Action, page 10. With regard to the quantity of experimentation, the Patent Office alleges that a great deal of experimentation is required because the specification does not teach whether the G80S mutation is found in normal individuals or whether the mutation is found only in affected patients. *Id.* Applicants respectfully disagree for at least the reasons provided above. In short, the specification provides that the G80S mutation, not known to be present in human ferroportin 1 gene sequences previously described, is carried in a particular family having a high incidence of non-HFE hemochromatosis, and that clinical traits associated with being a G80S carrier include higher than normal ferritinemia values. It is respectfully submitted that those diagnosed with hemoglobin and ferritinemia values outside of the normal range would find the recited polynucleotides of immediate benefit to ascertain for the possibility of being a G80S carrier, and thus, possibly at risk for non-HFE hemochromatosis similar to the family of G80S carriers. *See* Specification, page 9, lines 23-27. Consideration of the two *Wands* factors, the relative skill of those in the art and the quantity of experimentation necessary favors a finding of no undue enablement.

For at least the foregoing reasons, Applicants respectfully submit that the presently pending claims are fully enabled. Accordingly, Applicants respectfully request that the rejection of the presently pending claims under 35 U.S.C § 112, first paragraph, be withdrawn.

**X. CLAIM REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, FOR INDEFINITENESS**

---

Claims 1-4, 11-21, and 50-52 stand rejected under 35 U.S.C § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. The rejection of claims 2-3 is moot in view of the cancellation of the claims. Particular allegations by the PTO are addressed below.

*i. “isolated polypeptides”*

Claims 1, 4 and 50-51 stand rejected as indefinite over the recitation of “isolated nucleotides” allegedly because it is unclear whether multiple copies of the same polynucleotide are required or whether the several different polynucleotides that encode ferroportin 1 are required. Office Action, page 11.

Without acquiescing to the propriety of the rejection, and solely to expedite prosecution of the claims, Applicants have amended claim 1 to recite “An isolated polynucleotide.” Applicants respectfully submit that this rejection is obviated in view of the amendments to claim 1.

*ii. “the wild type sequence”*

Claims 1, 4 and 50-51 stand rejected as indefinite over the recitation of “the wild type sequence” allegedly because the term lacks proper antecedent basis. The Patent Office further alleges that it is unclear whether the claims require “the wild-type” sequence except have only one change at position 80 of SEQ ID NO:2 or whether the sequence may have many mutations with respect to the wild-type sequence. Office Action, pages 11-12.

Without acquiescing to the propriety of the rejection, and solely to expedite prosecution of the claims, Applicants have amended claim 1 to delete the phrase “as compared to the wild-type sequence.” Applicants respectfully submit that this rejection is obviated in view of the amendments to claim 1.

*iii. “characterized in”*

Claims 4, 11-21, and 52 stand rejected as indefinite over the recitation of “characterized in” allegedly because it is unclear whether the language is open or closed transitional language and what is encompassed by the claims. Office Action, page 12.

Without acquiescing to the propriety of the rejection, and solely to expedite prosecution of the claims, Applicants have amended claims 4, 11-21, and 52 to delete the phrases “characterized in” and “characterized by.” Applicants respectfully submit that this rejection is obviated in view of the amendments to the claims.

vi. “corresponds to”

Claims 14-17 and 52 stand rejected as indefinite over the recitation of “corresponds to” allegedly because it is unclear what the transition corresponds to encompasses. Office Action, page 12.

Without acquiescing to the propriety of the rejection, and solely to expedite prosecution of the claims, Applicants have amended claims 14-17 and 52 to delete the phrases “corresponds to” and “corresponding to.” Applicants respectfully submit that this rejection is obviated in view of the amendments to the claims.

v. “derived from”

Claims 15-17 stand rejected as indefinite over the recitation of “derived from” allegedly because this language does not particularly set forth whether the polynucleotides are limited to fragments of the SEQ ID NO:3 overlapping position 238 or can include sequences which were originally taken from SEQ ID NO:3 but are then modified. Office Action, page 12.

Without acquiescing to the propriety of the rejection, and solely to expedite prosecution of the claims, Applicants have amended claim 15 to delete the phrase “derived from.” Applicants respectfully submit that this rejection is obviated in view of the amendments to claim 15.

For the foregoing reasons, Applicants respectfully request that the rejection of claims 1, 4, 11-21, and 50-52 under 35 U.S.C § 112, second paragraph, be withdrawn.

**XI. CLAIM REJECTION UNDER 35 U.S.C. § 102(b)**

Claims 15 and 17 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Fodor (U.S. Publication No. 2001/0053519, December 20, 2001). The Patent Office alleges that Fodor teaches analysis using a 10-mer array and disclose results from the hybridization of a sample of DNA to an array containing all possible 10-mers, which was manufactured using photolithography techniques on an array. Office Action, page 13. The Patent Office contends that Fodor inherently teaches a polynucleotide carrying 10 consecutive nucleotides from SEQ ID NO:3 comprising at least one of polymorphic nucleotides corresponding to position 238 of SEQ ID NO:3 because Fodor teaches every 10-mer. *See Id.*

In order to anticipate the claimed invention, a single reference must teach each and every element of the claims. *Verdegaal Bros. v. Union Oil Co.*, 2 U.S.P.Q.2d 1051, 1052-53 (Fed. Cir. 1987).

Applicants respectfully traverse this rejection since Fodor does not teach each and every element of claims 15 or 17. Nonetheless, without acquiescing to the propriety of the rejection, and solely to expedite prosecution of the claims, Applicants have amended claim 15 to recite "An isolated polynucleotide comprising more than 10 consecutive nucleotides of SEQ ID NO:3". As such, Applicants respectfully submit that this rejection is obviated in view of the amendments to the claims.

Thus, Applicants respectfully submit that the presently pending claims are not anticipated by the reference cited by the Patent Office. Accordingly, Applicants respectfully request that the rejection of claims 15 and 17 under 35 U.S.C § 102(b) be withdrawn.

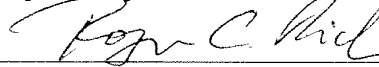
### **CONCLUSION**

In light of the above amendments and remarks, Applicants respectfully request that the Patent Office reconsider this application with a view towards allowance.

No fee is believed to be due with this paper other than the fee for a one-month extension of time in which to respond. However, the Commissioner is hereby authorized to charge any required fee(s) to Jones Day Deposit Account No. 50-3013 (order no. 043018-999116).

Date: February 26, 2009

Respectfully submitted,



Roger C. Rich

For: Nikolaos C. George

54,398

(Reg. No.)

(Reg. No. 39,201)

### **JONES DAY**

222 East 41st Street

New York, New York 10017

(212) 326-3939

**Appendix A**

Attached are seven replacement sheets of drawings for Figures 1-3 to be substituted for the corresponding drawing sheets presently on file in the above-identified application.